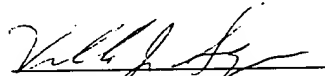


stomach.

There is no teaching, suggestion or incentive supporting the combination which the examiner proposes and even if the combination is made, there is nothing to teach or suggest utilization of different polymers or mixture of polymers combined with portions of the active ingredients for more uniform distribution of an active ingredient through the stomach. Consequently, absent a teaching, suggestion or incentive supporting the combination, the rejection is improper and should be withdrawn.

Based on the above amendments and remarks reconsideration and removal of the grounds of the rejection are respectfully request. However should the examiner believe that direct contact with the applicant's attorney would advance the prosecution of the application, the examiner is invited to telephone the undersigned at the number given below.

Respectfully submitted,



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AMENDED CLAIMS

2. Formulation according to claim 21 wherein such association of polymers or mixtures of polymers includes a polymer or mixture of polymers soluble starting from pH, a polymer or mixture of polymers soluble starting from pH 6.5, and a polymer or mixture of polymers soluble starting from pH 7.

3. Formulation according to claim 2 wherein release of the active ingredient in every phase occurs in the pH dependent ratios:

pH=6 ⇒ 10-60% of the active ingredient

pH=6.5 ⇒ 10-60% of the active ingredient

pH=7 ⇒ 10-60% of the active ingredient.

4. Formulation according to claim 21 wherein such active ingredient is mesalazine.

5. Formulation according to claim 21 wherein such active ingredient is chosen from the group including steroids, antibiotics and anti-inflammatories.

6. Formulation according to claim 21 in the form of micro-tablets, tablets, granules or microgranules or pellets of three types, each on presenting a coating including a polymer soluble starting from a pH value ranging from 6 to 7, such pH value being different for each of such three types.

10. Formulation according to claim 21 in the form of a multilayer tablet.

13. Formulation according to claim 21 in the form of tablets or multilayer tablets including, also in the tablet core and 5 to 35% of the polymer or mixture of polymers utilized in their coating, from 0 to 10% of a fatty acid at 12-20 carbon atoms and from 0 to 10% of a pharmaceutically acceptable plasticizer.

15. Formulations according to claim 21 wherein such polymer soluble starting from pH 6 is chosen from poly(methacrylic-co-methyl methacrylate), 1:1, 135,000MW or cellulose acetatephthalate or Hydroxypropylmethylcellulosephthalate or Hydroxypropylmethylcelluloseacetatesuccinate type L.

18. Formulation according to claim 21 wherein such mixture of polymers soluble starting from pH 6.5 is poly(methacrylic acid-co-methyl methacrylate), 1:1, 135,000 MW or Hydroxypropylmethylcellulosephthalate or Hydroxypropylmethylcelluloseacetatesuccinate type L in a mixture 1:1 with poly(methacrylic acid-co- methylmethacralate), 1:2, 135,000 MW.

19. Formulation according to claim 21 wherein such polymer soluble starting from pH 7 is poly(methacrylic acid-co-methacrylate), 1:2, 135,000 MW or poly(methylacrylate-co-methyl methacrylate-co-trimethacrylic acid), 7:3:1, 400,000 MW or Hydroxypropylmethylcellulosephthalate type M.

21. An oral solid formulation comprising an active ingredient in an amount sufficient to treat inflammatory bowel disease, portions of the active ingredient being combined with different polymers or mixtures of polymers, each polymer or mixture of polymers being soluble starting from a pH value different from each other polymer or mixture of polymers, for a multiphasic release of the portion of the active ingredient in combination therewith as each polymer or mixture of polymers is dissolved, each phase of release occurring at a different pH value corresponding to the pH values of the different polymers or mixture of polymers, ranging from a pH of 6 to 7.

22. Formulation according to claim 2 wherein release of the active ingredient in every phase occurs in the pH dependent ratios:

pH=6 ⇒ 30-35% of the active ingredient

pH=6.5 ⇒ 30-35% of the active ingredient

pH=7 ⇒ 30-35% of the active ingredient.

REPLACEMENT PARAGRAPH

Page 3, replace the paragraph extending from lines 21-26 with the following paragraph:

Document EP 0 629 398 (Tanabe Seiyaku Co. Ltd.) refers to pharmaceutical preparations able to provide a controlled release of the active ingredient in the desired zone of the intestinal tract (duodenum, small intestine, colon, rectum), and anyway at a $\text{pH} \geq 5$, through a proper choice of the coating, and checking, furthermore, the dissolution speed of the drug itself. Among the many coatings indicated as useful, Eudragit L, poly(methacrylic acid-co-methyl methacrylate), 1:1, 135,000 MW, available from Rohm Pharma polymers) and Eudragit S poly(methacrylic acid-co-methylmethacrylate), 1:2, 135,000 MW, available from Rohm Pharma Polymers are mentioned.

Data Sheet
for Registration

5. Scientific Names According to IUPAC Regulations

Type	Name(s)
EUDRAGIT[®] E	Poly(butyl methacrylate-co-(2-dimethylaminoethyl) methacrylate-co-methyl methacrylate) 1:2:1, 150,000, = polymer substance of EUDRAGIT [®] E 12,5, E 100, E PO
EUDRAGIT[®] NE 30 D	Poly(ethyl acrylate-co-methyl methacrylate) 2:1, 800,000, = polymer substance of EUDRAGIT [®] NE 30 D
EUDRAGIT[®] L	Poly(methacrylic acid-co-methyl methacrylate) 1:1, 135,000, = polymer substance of EUDRAGIT [®] L 12,5, L 100 Poly(methacrylic acid-co-ethyl acrylate) 1:1, 250,000, = polymer substance of EUDRAGIT [®] L 30 D-55*, L 100-55
EUDRAGIT[®] S	Poly(methacrylic acid-co-methyl methacrylate) 1:2, 135,000, = polymer substance of EUDRAGIT [®] S 12,5, S 100
EUDRAGIT[®] FS	Poly(methyl acrylate-co-methyl methacrylate-co-methacrylic acid) 7:3:1 (400,000), = polymer substance of EUDRAGIT [®] FS 30 D
EUDRAGIT[®] RL	Poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonioethyl methacrylate chloride) 1:2:0.2, 150,000, = polymer substance of EUDRAGIT [®] RL 12,5, RL 30 D, RL 100, RL PO, RD 100
EUDRAGIT[®] RS	Poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonioethyl methacrylate chloride) 1:2:0.1, 150,000, = polymer substance of EUDRAGIT [®] RS 12,5, RS 30 D, RS 100, RS PO
PLASTOID[®] B	Poly(butyl methacrylate, methyl methacrylate) 3:1, 150 000

The ratio indicates the molar proportions of the monomer units and the last figure the molecular weight of the polymer.

* formerly EUDRAGIT[®] L 30 D

Our technical advice on the applications of our products is given without obligation. The buyer is responsible for the use and processing of our products and is also liable for observing any third-party rights. Technical data concerning our products are typical values. Subject to alteration.

® = registered trademark

EUDRAGIT® = reg. Trademark of Röhm GmbH & Co. KG, Darmstadt, Germany